ADDENDUM TO CLINICAL REVIEW

Application Type	NDA
Application Number(s)	22-502
Priority or Standard	Standard
Submit Date(s)	February 27, 2009
Received Date(s)	March 2, 2009
PDUFA Goal Date	January 2, 2010
Reviewer Name(s)	Amy Woitach, D.O.
Review Completion Date	March 2, 2010
Established Name	Adapalene Lotion, 0.1%
(Proposed) Trade Name	Differin Lotion, 0.1%
Therapeutic Class	Naphthoic acid/ Retinoid
Applicant	Galderma Laboratories LP
Formulation(s)	Topical lotion
Dosing Regimen	Once daily
Indication(s)	Acne vulgaris
Intended Population(s)	12 years and older

Galderma submitted an original NDA on March 2, 2009 for Differin (adapalene) Lotion 0.1% for the treatment of acne vulgaris. The clinical review was closed on November 12, 2009. Inspections of manufacturing facilities were pending at the time of the close of the review. Labeling negotiations were also ongoing.

Inspections of Manufacturing Facilities:
On December 18, 2009 the Office of Compliance issued an overall recommendation of "*withhold*" based on the inspection of the (b) (4) back-up facility. Inspectors determined the facility was not ready for inspection. The sponsor was notified of the recommendation to withhold the approval by teleconference on December 22, 2009. On December 23, 2009 the sponsor submitted an amendment to remove the facility from the application. The amendment is considered a major amendment and extends the review clock by 3 months with a new PDUFA date of April 2, 2009. Based on the amendment, the Office of Compliance has issued a recommendation of "*acceptable*" on January 14, 2010.

Labeling Negotiations:
A labeling amendment was submitted on October 22, 2009, to provide the Agency with colored mock ups of the container/closure systems. In addition to draft carton and container labels for 2 ounce and 4 ounce trade sizes with pumps, (b) (4) . The sponsor confirmed that clinical trials were conducted with the pump configuration. A teleconference between the Agency and the sponsor was held on November 23, 2009 in which the FDA stated that:

> (b) (4) *The Agency will continue its review and action based only on the product described for use with the pump, because this was the drug product design used in the pivotal Phase 3 studies.* (b) (4)

(b) (4)

The Agency initiated a second teleconference in which the sponsor confirmed that clinical trials were conducted with the pump inserted into the bottle prior to dispensing to subjects. (b) (4) The Agency requested that the sponsor submit color mock ups of carton and container labels and provide instructions to the pharmacist; Galderma submitted this information in amendment on December 1, 2009.

DMEPA reviewer Lori Cantin provided draft comments to the Division stating that labeling is not likely to prevent the dispensing of the (b) (4) configuration.

Reviewer comment: This reviewer recommends approving the assembled configuration, with the pump inserted into the bottle, so that the configuration and dosing is consistent with that used in the phase 3 trials. (b) (4)

The Agency initiated a teleconference on January 28, 2010 to inform the applicant that the (b) (4)

With the Office of Compliance issuing an overall recommendation of "*acceptable"* and the resolution of labeling issues the CMC reviewer is recommending approval of this NDA.

Reviewer comment: This reviewer concurs and recommends approval of the NDA.

Labeling negotiations are complete. The revised carton and container labeling was deemed acceptable. The agreed upon label is appended to this review.

10 Page of Draft Labeling as been withheld in full after this page as B4 (CCI/TS)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22502	ORIG-1	GALDERMA RESEARCH AND DEVELOPMENT INC	DIFFERIN LOTION

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/s/

AMY S WOITACH
03/03/2010

DAVID L KETTL
03/03/2010
Concur with approval recommendation as CMC issues have been resolved.